Autoimmunity checkpoints as therapeutic targets in B cell malignancies.

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Public Summary:
Targeted therapy of cancer typically focuses on inhibitors (for example, tyrosine kinase inhibitors) that suppress oncogenic signalling below a minimum threshold required for survival and proliferation of cancer cells. B cell acute lymphoblastic leukaemia and B cell lymphomas originate from various stages of development of B cells, which, unlike other cell types, are under intense selective pressure. The vast majority of newly generated B cells are autoreactive and die by negative selection at autoimmunity checkpoints (AICs). Owing to ubiquitous encounters with self-antigen, autoreactive B cells are eliminated by the overwhelming signalling strength of their autoreactive B cell receptor (BCR). A series of recent findings suggests that, despite malignant transformation, AICs are fully functional in B cell malignancies. This Opinion article proposes targeted engagement of AICs as a previously unrecognized therapeutic opportunity to overcome drug resistance in B cell malignancies.

Scientific Abstract:
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